Amendments To The Specification:

Please amend the Specification to read as follows:

Replace paragraph [00003] in the Specification of the above-identified application with the following paragraph:

[00003] Throughout the history of human medicine, various compounds have been used for the relief of pain. In particular, a class of compounds of plant origin known as opiates have been used since prehistoric periods for analgesic and euphoric purposes. Even today the opiate drug morphine is used as an analgesic for significant pain, and morphine is still an important benchmark for clinical studies. Morphine is the most widely prescribed injectable opioid today, despite its narcotic side effects. Acute opioid toxicity from overdose can result in respiratory depression and death, whereas chronic use can ~~let~~ lead to physical dependence, addiction, and severe ~~sever~~ constipation.

Replace paragraph [00017] which includes Table 1 on page 5 of the Specification with the following paragraph:

[00017] Enkephalin and endorphin peptides may be thought of as having both ~~an~~ a message segment and an address segment. The message segment is portion of the molecule that binds to the receptor and is quite small, typically being the four amino acid motif YGGF (SEQ ID NO:1) in native enkephalins. The address portion appears to control membrane binding and may serve to help modify receptor specificity. As is well known, there are several classes of opioid receptors, with the three accepted subtypes being known as by the classifications mu (μ), delta (δ), and kappa (κ), with the corresponding clones receptors MOR, DOR and KOR. It is known that various endorphins and enkephalins bind preferentially to different classes of receptors. A listing of some endorphins and enkephalins (with single letter amino acid designations) and the receptors to which they bind is presented as Table 1 below. The message segments are underlined.

Table 1. Naturally Occurring Opioid Peptide Sequences.

Peptide	*Sequence*	*Subtype*
Met-Enkephalin	YGGFM (SEQ ID NO:2)	μ/δ
Leu-Enkephalin	YGGFL (SEQ ID NO:3)	δ/μ
Dynorphin A	YGGFLRRIRPKLKWNNQ (SEQ ID NO:4)	κ(μ)
Dynorphin B	YGGFLRRQFKVVT (SEQ ID NO:5)	κ(μ,δ)
α-Neoendorphin	YGGFLRKY (SEQ ID NO:6)	κ(μ,δ)
β-Neoendorphin	YGGFLRKYP (SEQ ID NO:7)	κ(μ,δ)
β_h-Endorphin	YGGFMTSEKSQTPLVTLFKNAIIKNAYKKGE (SEQ ID NO:8)	μ/δ
Peptide E	YGGFMRRVGRPEWWMDYQKRYGGFL (SEQ ID NO:9)	μ/κ
Peptide F	GGEVLGKRYGGFM (SEQ ID NO:10)	—
Nociceptin	FGGFLRRIRPKLKWNNQ (SEQ ID NO:11)	ORL
Deltorphin	YmFHLMD-$CONH_2$ (SEQ ID NO:12)	δ
Dermorphins	YaFGYPS-$CONH_2$ (SEQ ID NO:13)	μ
Morphiceptin	YPFP-$CONH_2$ (SEQ ID NO:14)	μ
β-Casomorphin	YPFPGPI (SEQ ID NO:15)	μ
Endomorphin-1	YPWF-$CONH_2$ (SEQ ID NO:16)	μ
Endomorphin-2	YPFF-$CONH_2$ (SEQ ID NO:17)	μ
Rubiscolin-6	YPLDLF (SEQ ID NO:18)	δ

Replace paragraph [00018] in the Specification of the above-identified application with the following paragraph:

[00018] The classic motif for opioid receptor binding is the YGGF (SEQ ID NO:1) sequence. While some variations are possible in this motif, it appears that the first tyrosine and the fourth phenylalanine are invariant requirements of enkephalins. The discovery of natural opioid peptides in the skin of the frog *Phyllomedusa bicolor*, which naturally produces the enantiomeric D-amino acids, led to investigations of other D-amino acids which can substitute for the glycine intermediate residues in the motif. In particular, the several motifs with a D-amino acids, including Tyr-D-Cys-Gly-Phe (SEQ ID NO:19), Tyr-D-Ala-Gly-Phe (SEQ ID NO:20), and Tyr-D-Thr-Gly-Phe (SEQ ID NO:21) have been found effective synthetic enkephalin message sequences. Synthetic enkephalin analogues with a D-amino acid substituted for the first glycine have been designed to bias the conformation of the

molecule to obtain greater affinity for opioid receptors. Note that in the Table 1 above and 2 below that the small case letter designation refers to a D-amino acid, such as "t" referring to D-Thr.

Replace Table 2 in the Specification of the above-identified application with the following:

TABLE 2

Receptor Binding Characteristics

ID Code	Message	Address (Transport Sequence)	Delta nM	MU nM	MVD nM	GPI nM	ICV(Mouse) IC50 nmol	IV(Mouse) µmol/kg	+ Err (95%) µmol/kg
Morphine	Morphine	Morphine					2.7	6.3	4.9-7.9
SAM 995	YtGFL	S-CONH2 (SEQ ID NO:22)	2.1	7.5	2.723	25.04	0.07	46.4	35.4-60.7
SAM 1095	YtGFL	L-Ser (b-Glc) CONH2 (SEQ ID NO:23)	2.37	7.63	1.56	33.83	0.02	11.4	8.5-15.2
MMP 2120	YtGFL	L-Ser (a-Man) CONH2 (SEQ ID NO:24)	22.95	15.2	3.029	23.25	0.04	31.6	26.5-37.8
MMP 2200	YtGFL	L-Ser (b-Lactose) CONH2 (SEQ ID NO:25)	17.3	40	5.727	34.75	0.02	3.2	2.5-4.2
MMP 2205	YtGFL	L-Ser, L-Ser (b-Glc) CONH2 (SEQ ID NO:26)			1.169	53.51	0.3	140.8	78-253.9
MMP 2230	YtGFL	L-Ser (b-Maltose) CONH2 (SEQ ID NO:27)	9.86	30.8	1.705	52.57	0.07	~12	-
MMP 2300	YtGFL	L-Ser (b-Maltotriose) CONH2 (SEQ ID NO:28)	3.8	15	7.73	71.73	0.06	10.9	8.5-13.9
CM 100	YtGFL	L-Ser (b-Xyl) CONH2 (SEQ ID NO:29)					~0.04	9.45	8.34-10.71
MD 2005	YtGFL	L-Ser (b-Melibiose) CONH2 (SEQ ID NO:30)	5.6	36.6			0.034	2.16	1.84-2.53
MD 100H	YtGFL	PNLBEKALKS*L-CONH2 (SEQ ID NO:31)					~0.03		
MD 105H	YtGFL	(beta-Ala)NLBEKALKS*L-CONH2 (SEQ ID NO:32)	47.3	62.1			~0.03		
MD 110H	YtGFL	GGNLBEKALKS*L-CONH2 (SEQ ID NO:33)	35	81			~0.03		

Replace paragraph [00024] in the Specification of the above-identified application with the following paragraph:

[00024] It is anticipated that the glycosylated enkephalins of the present invention will prove useful clinical drugs for analgesia and anti-depression. For clinical use, the glycosylated peptides would be made in suspension and packaged and labeled with suitable instructions for use with patients. The drugs could be delivered intravenously and still bind to the appropriate receptors in the brain, due to the passage of the molecules through the blood-brain barrier. Other adjuvants, additives and potentiating factors might also be ~~includes~~ included in such formulations.

Enter the Sequence Listing included with this submission into the Specification of the above-identified application.